

## REMARKS

This paper is submitted in response to the office action mailed November 14, 2008, in connection with the above-identified application (hereinafter, the "Office Action"). The Office Action provided a three-month shortened statutory period in which to respond, ending on February 14, 2009. Submitted herewith is a Petition for a Three-Month Extension of Time extending the due date to May 14, 2009 and a Request for Continued Examination Transmittal Form. Accordingly, this Response is timely submitted.

Claims 1 through 21 are currently pending. Claims 1 through 21 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Cimarelli et al. (Tetrahedron: Asymmetry (2002, 13(22), 2417-26) (hereinafter "*Cimarelli*"). Applicants respectfully disagree with this rejection by the Examiner and request withdrawal of the pending obviousness rejection.

*Graham v. John Deere Co. of Kansas City*, 383 U. S. 1, 17-18 (1966), establishes an objective analysis for applying §103 to a question of obviousness: "the scope and content of the prior art are . . . determined; differences between the prior art and the claims at issue are . . . ascertained; and the level of ordinary skill in the pertinent art resolved." The USPTO bears the burden of establishing a *prima facie* case of obviousness based on the results of the factual inquiries under *Graham*. The *prima facie* case generally requires three showings: 1) some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings; 2) a reasonable expectation of success; and 3) that the prior art reference or combination of references teaches or suggests all the claim limitations. MPEP §2143.

The Applicants respectfully submit that a *prima facie* case of obviousness has not been established. A *prima facie* case of obviousness must establish some apparent reason why one would modify the expressly disclosed compounds to achieve the compounds expressly claimed in the present invention. See *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1741 (citing *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006))('[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.') According to the Supreme Court, a proper case of *prima facie* obviousness must be articulated to a patent application by setting forth the reasoning and underlying rationale used to arrive at a legal conclusion of obviousness. *Id.*

In the prior Office Action, the Examiner previously stated that "one having ordinary skill in the art at the time that applicant's invention was made would have had a reasonable expectation of success in using structurally obvious compounds to those disclosed in *Cimarelli* in a process of making chiral alcohols." The Examiner presently restates that the present invention is

deemed to be obvious based upon the alleged structural similarity to the Cimarelli compounds and lack of side-by-side comparison.

Applicants respectfully submit that one of ordinary skill would not derive the present invention from *Cimarelli* due to significant differences regarding the structure and the uses of the claimed and *Cimarelli* compounds. In the present invention, chiral tertiary aminoalkylnaphthols are used as chiral ligands for the enantioselective arylation of aldehydes. These chiral tertiary aminoalkylnaphthols include different substituents and different structure than *Cimarelli*.

Contrasted to the present invention, *Cimarelli* describes the use of secondary aminonaphthols for the enantioselective alkylation of aldehydes. *Cimarelli* teaches away from the present invention by disclosing that tertiary aminonaphthols do not afford better catalytic activity than their secondary aminonaphthols and, in fact, frequently experienced a moderate spontaneous epimerization. (*Cimarelli et al.*, *Tetrahedron: Asymmetry*, 2002, 13: 2417-2426, at pp. 2420-21.) This epimerization issue in *Cimarelli* became more important when the steric hinderance from the *N*-substituent increased. (*Id.*)

In the present invention, the newly introduced bulky naphthyl group attached to the new chiral center may favor selection of conformationally more restricted transition state, which should be beneficial for stereochemical induction (figure 1).

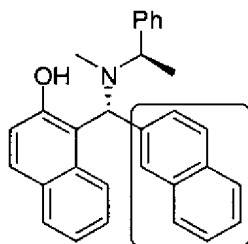


figure 1

However, it may also shut down the reaction altogether because of the excess of steric hindrance. As supported by *Cimarelli*, it is well-established that different substitutions cause different stereochemical results. Contrary to the Examiner's assertion, the presumption of obviousness based upon the allegedly structurally similar compounds would be overcome since there is sufficient evidence showing there is no reasonable expectation of similar properties in structurally similar compounds. (See M.P.E.P., Eighth Edition, Revision 7, §2144.09.) Contrary to the Examiner's assertion, Applicants assert that one of ordinary skill would not ignore these teachings in *Cimarelli* and would not derive the chiral tertiary aminoalkylnaphthol compound of the present invention or their claimed use for the enantioselective alkylation of aldehydes from the teachings of *Cimarelli*.

Furthermore, Applicants note that the present invention features the use of the claimed compounds for the enantioselective arylation of aldehydes which is different from *Cimarelli*. In

contrast, *Cimarelli* teaches the use of its disclosed compounds for the enantioselective alkylation of aldehydes. These two kinds of reactions are fundamentally different.

It is well-established that various zinc reagents including alkyl-, aryl-, alkenyl-, and alkynylzincs showed very different characteristics in reactivity and stereochemical selectivity. See Yu et al., *Chem. Rev.*, 2001, 101, 757-824. Even though several chiral ligands were disclosed for the asymmetric alkylzinc addition to carbonyl compounds, ligands which effectively catalyze the aryl transfer reactions to arylaldehydes with high ee values are rare before the present invention. Earlier known catalysts focused on planar-chiral ligands, which were prepared from cumbersome synthetic steps. Using chiral tertiary aminoalkynaphthol ligands to effectively catalyze the aryl transfer to arylaldehydes, the present invention established a convenient method for achieving high enantioselectivity in these useful reactions. Further, these chiral ligands are surprisingly simple and easy to use, for example, in the one-pot direct condensation of three readily available components to yield the desired aminonaphthol with good diastereoselectivity. The present invention is a significant breakthrough in the catalytic aryl-transfer to arylaldehydes in an enantioselective manner. For the foregoing reasons, Applicants respectfully submit that the present invention is not rendered obvious under 35 U.S.C. §103(a) by *Cimarelli*.

Applicants respectfully submit that Claims 2-5 and 7-21 are in condition for allowance as they depend from an allowable independent base claim.

In view of the foregoing arguments, Applicants respectfully request that the claims of the present application be reconsidered. If a telephone interview would be of assistance in advancing the prosecution of this application, Applicants' undersigned attorney invites the Examiner to telephone him at the telephone number provided below.

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Respectfully submitted,

  
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